REMARKS

Claims 3-8, 14, 18, 32-34, 42-52, 54, 63, 64, 72, 73, 79-83 have been canceled, without prejudice.

Claims 1, 2, 9-13, 15-17, 19-31, 35-41, 53, 55-62, 65-71, 74-78, 84-112 are now pending in the application.

Claim 1 was amended to improve the readability of the claim and to correct errors in antecedence. Also, the recitation of "live cells" and the reference to mixing on a molecular level have been deleted. This claim was also amended recite that the pectin is an Aloe pectin. Support for this amendment can be found in the specification at, *inter alia*, page 31, line 9, to page 33, line 3, and Claim 14. As a result of this amendment, Claim 14 was canceled and Claims 9-13, 15-16, and 112 were also amended to recite proper antecedence. Claim 1 was also amended to recite that the Aloe pectin is "present in an amount of about 0.25% to about 2%, based on the total weight of the composition." Support for this amendment can be found in the specification at page 36, line 18.

Claim 22 was amended to remove overlap with Claim 23.

Claims 24-25 were amended to correct errors in antecedence with base Claim 1.

Claim 27 was amended to improve the readability of the claim and to correct errors in antecedence.

Claim 30 was amended to remove overlap with Claim 31.

Claim 53 was amended to improve the readability of the claim and to correct errors in antecedence. Also, the recitation of "live cells" and the reference to mixing on a molecular level have been deleted. Claim 53 was also amended to recite that the pectic substance is "present in an amount of about 0.25% to about 2%, based on the total weight of the composition." Support for this amendment can be found in the specification at page 36, line 18.

Claim 69 was amended to remove overlap with Claim 70.

Claim 71 was amended to correct a typographical error. Support for this amendment can be found in the as-filed specification in Table 1, at page 22.

Claim 78 was amended to improve the readability of the claim.

Claim 95 was amended to remove overlap with Claim 96.

Claim 111 was amended to improve the readability of the claim and to correct errors in antecedence. Also, the recitation of "live cells" and the reference to mixing on a molecular level

have been deleted. Claim 111 was also amended to recite that the pectic substance is "present in an amount of about 0.25% to about 2%, based on the total weight of the composition." Support for this amendment can be found in the specification at page 36, line 18.

No new matter has been added by these amendments; therefore, examination is requested on the claims as amended herewith.

Rejections Under 35 U.S.C. § 103

The Office Action alleged that all of the pending claims are obviousness under 35 U.S.C. § 103 in view of various references, including Baichwal (U.S. Patent No. 5,612,053), Watts (U.S. Patent No. 6,310,089), and Ni (U.S. Patent No. 5,929,051), as well as others. Applicants respectfully traverse these rejections to the extent they apply to the claims as amended herewith.

The Office Action's first and main contention is that it would have been obvious for the skilled artisan to use the pectins of Ni or Watts in the compositions and methods of Baichwal in order to arrive at the claimed invention. Specifically, Baichwal discloses a powder composition for the delivery of drugs to the respiratory tract and nasal passages. Baichwal further discloses that its compositions have a polysaccharide carrier of natural origin. However, Baichwal neither specifies pectins in general nor mentions any particular pectins for use as a carrier in its compositions. For this missing element, the Office Action turned to Watts and, more specifically, Ni, which disclose pectins as drug delivery carriers. As such, the Office Action concluded that it would have been obvious to simply substitute the pectins of Ni or Watts as carriers in Baichwal's compositions and thereby produce the presently claimed invention.

Standard for obviousness

It is helpful to first consider the standards for obviousness as recently articulated by the Supreme Court in *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727 (April 30, 2007). In essence, the Office Action contended that the invention, as defined in the current claims, consists of the substitution of one known element for another to yield predictable and inherent results. As the recent Examiner Guidelines for handling obviousness rejections under *KSR* note, Applicants may respond to such objections by showing, for example, that the elements in combination do not merely perform the function that each element performs separately. MPEP § 2141(v).

Accordingly, when considering obviousness of a claimed combination of known elements, the operative question is whether the claimed invention "is more than the predictable use of prior art elements according to their established functions." (Fed. Reg. 72(195):57526

(October 2007), citing *KSR*). Applicants respectfully submit that, when viewed in the light of *KSR*, it is clear that the claimed invention meets the criteria for non-obviousness in that the pectins recited in the claimed compositions and methods are not merely carriers or excipients performing their predicted function; instead, they are agents present in a specific amount that produce a unique function not appreciated by the cited references (*i.e.*, *in situ* gelation).

Turning to the teachings of the cited references, Baichwal discloses controlled release dry powder formulations for delivery of actives to nasal and respiratory tissue. Baichwal teaches that its dry powder formulations contain a homo- or hetero-polysaccharide carrier of natural origin (col. 5, l. 54, to col. 6, l. 43). Baichwal provides a list of suitable carriers, but pectins are absent and nowhere mentioned. Baichwal does not teach a dry powder formulation that gels *in-situ*. Watts, in contrast, discloses aqueous liquid compositions for delivery of actives to the nasal tissue that gel *in situ*. Watts discloses that its compositions contain "excipients" and lists pectins as one of many examples (col. 2, lines 59-64). Ni discloses specific low methoxyl pectins for use in the delivery of various actives. The pectins of both Watts and Ni are, of course, hetero-polysaccharides of natural origin.

The Office Action has alleged that it would have been obvious to use the pectins of Ni or Watts in the formulations of Baichwal, thereby arriving at the claimed invention. However, this allegation overlooks the fact that in order to arrive at the claimed invention, the skilled artisan would have had to first begin with the notion of an *in-situ* gelling solid, which is a concept not previously disclosed. At best Watts discloses a gel substance can be formed from an aqueous solution; it was not previously known that a gel can be formed from a solid upon contact with a body fluid (nasal fluid) or *in-situ*. Such a starting point is ignored by the Office Action, alleging only that the skilled artisan would have simply (and perhaps haphazardly) substituted just any pectin (as in Watts) or the specific pectins of Ni into Baichwal's formulations, thereby inherently arriving at the present invention as if by accident.

Also, notably missing from all of the cited references is the fact that the specific pectins recited in the claims gel in certain concentrations when contacted to certain tissues and fluids (*i.e.*, *in situ* gelation). This fact, identified by Applicants, translates into several unique features recited in the claims, namely, the type and amount of pectins used. So even if the skilled artisan would have (for some reason) combined the pectins of Watts or Ni into the formulations of

Baichwal, the combination would not have arrived at the present invention, as recited in the amended claims.

1. The type of pectins

The amended claims recite a composition that contains specific pectins, *i.e.*, low methoxyl (DM<50%) pectins. Thus, the skilled artisan would have to deviate from the teachings of Baichwal by ignoring the list of polysaccharide carriers in the reference and choosing pectin, a polysaccharide carrier that is not mentioned. Not only that, but the skilled artisan would also have to select the specific low methoxyl Aloe pectins recited in the claims, as opposed to another pectin like apple, citrus, or other high methoxyl pectins. Choosing the specific low methoxyl pectins recited in the claims from among the countless choices of polysaccharide carriers described in Baichwal, Watts, Ni and elsewhere speaks to the non-obviousness of the claimed compositions.

Moreover, Applicants' Example 27 (p. 71 *et seq.*) compares various low methoxyl pectins for *in situ* gelation in the nasal cavity. As is shown, Aloe pectins have the largest gel area, from 6.5 to 33 times larger than that of the other low methoxyl pectins. Thus, without Applicants' own teachings in the present application that the recited pectins form gels *in situ*, and to a much greater extent than other albeit similar low methoxyl pectins, the skilled artisan would have no articulable reason to use the recited low methoxyl pectins in the claimed compositions. In other words, while the Office Action might contend that it would have been obvious to substitute pectins in general into the formulations of Baichwal, there is no reason, other than Applicants own teachings, to use the specific low methoxyl pectins recited in the claims as opposed to the typical high methoxyl pectins.

2. The specific amount of pectin

The current claims have also been amended to recite that the amount of low methoxyl pectin is from about 0.25 % to about 2% by weight of the total composition. Such amounts are nowhere suggested or disclosed in the cited reference. Thus assuming, *arguendo*, the skilled artisan would have been motivated to select the pectins of Ni or Watts and use them in the formulations of Baichwal (which they wouldn't have), the resulting combination would not have resulted in the claimed invention. In particular, Baichwal, Watts, and Ni all describe compositions where the polysaccharide carrier (whether it be pectin or otherwise) is present in amounts much higher than that recited in the claims.

The amount of polysaccharide carrier disclosed in Baichwal is "from 10% to 99.9%, more preferably 50 % to 99.9%" (*see* col. 4, ll. 1-6). See also Baichwal's Example 1 where 60 g of carrier is combined with 16 g of active, which equals 79% carrier by weight of the total composition. A similar calculation for Baichwal's Example 3 yields 73% carrier by weight of the total composition.

Both Watts and Ni disclosed the aqueous liquid formulations. When water is removed from the formulation to produce the dry powder formulation, the percent content of dissolved substances is substantially increased. Thus, Ni discloses active-containing compositions where pectin is the major component (*see* Example 14 where pectin is above 99% by weight of the composition after drying or removing water). Watts discloses that its excipients, pectins being one of a laundry list of examples, are present at from about 5% to 95% of the composition as a liquid (*see* col. 3, ll. 57-60), or above 90% after removing water. Thus, the alleged obvious combination of the teachings of these references would result in a composition where low methoxyl pectin would be present at a much higher amount than that recited in the present claims (at least 5 x as much, and likely much more).

Moreover, Applicants' Example 6 (p. 45) compares various concentrations of Aloe pectins for *in situ* gelation over time. It was found that the lower the pectin concentration the faster the gelation (*see also* Figure 2). Further, the addition of other polymers, which might be expected to interfere with the pectin's ability to gel, had little to no effect on gelation (*see* Example 7). Accordingly, the claims recite a specific amount of specific pectins that result in a composition that can accommodate other polymers while still gelling at a fast rate. As such, the claimed compositions remain in contact with tissues for a longer period of time; this is particularly beneficial for nasal drug delivery.

Because the Office Action has not articulated any reason that the skilled artisan would have been motivated to prepare an *in-situ* gelling solid, then look to pectins, then chose the specific low methoxyl Aloe pectins recited in the claims, and then use those pectins in the 0.25 to 2% amount recited in the claims, the claims are not obvious over the cited references.

The Office Action next alleged that Claims 20, 21, 25, 26, 30, 31, 69, 70, 75-78, 90, 91, 111, and 112 are obviousness under 35 U.S.C. § 103 in view of Baichwal, Watts, Ni, and in further view of Kuo (U.S. Patent No. 6,518,239), Gordon (U.S. Patent No. 2,629,665), or

Mizushima (U.S. Patent No. 5,942,242). Applicants respectfully traverse these rejections to the extent they apply to the claims as amended herewith.

These rejections are essentially the same as the rejection outlined above; however, the Kuo reference was included for its teachings of vaccine delivery by inhalation, the Gordon reference was included for its teaching of calcium ions to induce gelation of pectins, and the Mizushima reference was included for its teachings of thickeners. Applicants respectfully submit that for the same reasons outlined above, these claims are not rendered obvious by this combination of references. That is, none of the cited references suggest a composition with the specific type and amount of pectin recited in the present claims—a type and amount which Applicants have shown produces the beneficial effect of *in situ* gelation.

Double Patenting Rejection

The Office Action also rejected the present application on the ground of obvious-type double patenting over claims 1-70 of Ni (U.S. Patent No. 5,929,051) in view of Baichwal and Watts, and in further view of Kuo, Gordon, and Mizushima. Applicants respectfully traverse this rejection. As noted above, while Ni does disclose low methoxyl Aloe pectins that gel in the presence of calcium, there is nothing to suggest that they be used as a solid and in the amounts recited in the present claims. Thus, for much of the reasoning above, the current claims are not obvious in view of Ni in view of Baichwal and Watts, or in further view of Kuo, Gordon, and Mizushima.

CONCLUSION

Applicants respectfully submit that all outstanding objections and rejections stated in the Office Action have been overcome and should be withdrawn. Accordingly, the application is believed to be in condition for allowance and Applicants respectfully request issuance of a Notice of Allowance.

A credit card payment submitted via Form PTO-2038 in the amount of $1230.00 is enclosed. This payment includes the $180.00 fee for the Supplemental IDS under 37 C.F.R. § 1.97(c)(2) and 37 CFR § 1.17(p) and the $1050.00 fee for the Three-Month Extension of Time under 37 C.F.R. § 1.17(a)(3). No additional fees are believed to be due; however, the Commissioner is hereby authorized to charge any fees which may be required or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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Christopher L. Curfman, JD, PhD

July 16, 2008
Date